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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/522,799

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Mutsumi Takagi

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WASHINGTON, DC 20006-1021

EXAMINER

BOBBS, MICHAEL L

ART UNIT

PAPER NUMBER

1797

MAIL DATE

DELIVERY MODE

12/11/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/522,799

Applicant(s)

TAKAGI ET AL.

Examiner

MICHAEL HOBBS

Art Unit

1797

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 August 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-24, 26-29 and 31-39 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-24, 26-29 and 31-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicant's amendment filed on 08/18/2008 has been considered and entered for the record. Applicant's amendment overcomes the claim objection in paragraph 2 of the Office Action mailed on 03/17/2008 and overcomes the 35 USC 112 second paragraph rejection in paragraph 4 of the Office Action mailed on 03/17/2008. Also, Applicant's amendment overcomes the 35 USC 102(b) rejection in paragraph 8 of the Office Action mailed on 03/17/2008. Claims 21-24, 26-29 and 31-39 are pending further examination upon the merits.

Claim Objections

2. Claim 21 is objected to because of the following informalities: in part (f) of the culture apparatus, the claim reads a "united for controlling" which the Examiner is assuming the Applicant meant a "unit for controlling" and will interpret the claims accordingly. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 21 recites the limitation "the culture container" in line 5. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 21, 26-28, 33 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pieler et al. (WO0 91/01365) and in view of Hutchins et al. (US 5,955,373).

10. Pieler discloses an automated culture system that includes an incubator (incubator 112), a liquid handling station (station 134) and a robot (robot 136) that transfers the cells from the incubator to a fluid handling station. The incubator includes a housing enclosing a sub-divided interior space (page 11 lines 6-8). The sub-divided interior space includes separate compartments (compartments 116, 118, 120, 122) and is used to maintain the cell trays at prescribed conditions, such as 37 °C, a relative humidity of nearly 100% and a 5% concentration by volume of carbon dioxide (page 11 lines 20-23). The transport means is a robot that moves the plates or containers to and from the different stations, i.e. fluid transfer and the incubator. The robot removes a plate from the incubator to the fluid transfer station and then places the cells back into the incubator. After a prescribed period of time, the robot transfers the cells to a luminometer (luminometer 161) for optical testing (page 11 lines 6-12, 28-31; page 12 lines 10-14). Pieler discloses a humidity control means or a unit for monitoring the culture conditions within the incubator (page 29 lines 11-12). Finally, Pieler discloses a computer which is fully capable of receiving a signal from the humidity control means or any monitoring unit and adjusting the conditions within the incubator accordingly (page

lines 32-34). Pieler is silent regarding a window for the incubator and a "practicable door".

11. Hutchins discloses an environmentally controlled system for processing chemical products that includes a multiple inter-connected work stations covered with a canopy and a transport system for moving products within a chamber and between workstations. For claim 21, Hutchins discloses that there are multiple work stations such as a corner unit (corner unit 12a), an assay product entry unit (product unit 12b), a washing unit (unit 12c) and an incubator unit (incubator 12d; col. 3 lines 47-50). Furthermore, the units are divided into separate units (see Fig. 1 & Fig. 2) and a transport system (robot 23) moves the product from one work station to another (col. 3 line 65 - col. 4 line 3). Based on Fig. 3, Hutchins discloses that the work stations are divided by a wall (wall 18) and includes an entry door (door 24) between each unit. The canopy of Hutchins is being interpreted as being transparent in order to provide a window to observe the incubator and Hutchins discloses an assay supply section (supply 25) that is fully capable of supplying a culture media to the containers. It would be obvious to one of ordinary skill in the art to employ the enclosed workstations suggested by Hutchins in order to seal off the processes of Pieler. The suggestion for doing so at the time would have been in order to alleviate problems caused by changing environmental conditions during certain portions of the process such as variations of environmental conditions caused by opening an incubator for insertion or removal (col. 1 lines 39-41 & 59-61).

12. For claims 26 and 27, Pieler discloses a washing and supply stations as discussed above. Furthermore, the robot of Pieler is fully capable of intermittently transferring the containers between the different units and the computer of Pieler is being interpreted as the instruction controlling unit. For claim 33, the container of Pieler is fully capable of being disposable or "not reused".

13. Regarding claim 36, Pieler discloses a luminometer (luminometer 161) for optical testing (page 11 lines 6-12, 28-31; page 12 lines 10-14) that is fully capable of performing a cell count and is being interpreted as a "non-invasive" measurement apparatus.

14. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pieler et al. (WO0 91/01365) and in view of Hutchins et al. (US 5,955,373) and in further view of Rodgers et al. (US 2005/0037485 A1).

15. Pieler and Hutchins disclose means of transferring fluid, but are silent regarding a syringe.

16. With regards to claim 34, Rodgers discloses a fluid transfer station that uses a syringe to deliver the fluid ([0077]) and it is an intrinsic property of the syringe that it would be sterile. The use of a syringe is one of a finite means of either delivering or removing material from a culture container such as a pipette, needle, micro-pipette, or tube. Therefore, it would have been obvious to one of ordinary skill in the art to employ

the syringe as suggested by Rodgers within the supply station of Pieler and Hutchins with a reasonable expectation of success.

17. Claims 22 and 23 rejected under 35 U.S.C. 103(a) as being unpatentable over Pieler et al. (WO0 91/01365) in view of Hutchins et al. (US 5,955,373) and in further view of Creed (US 4,666,722).

18. For claims 22 and 23, Rodgers and Hutchins are silent regarding introducing a sterile gas to the portions of the box or that the sterile gas is ozone.

19. For claim 22, Creed discloses that cars containing package-laden trays are sent to an unloading station where the trays are removed by the clamping and transfer device (col. 3 lines 2-5). Furthermore, the cars are sent to the sterilizing apparatus and after the doors to the apparatus are closed and locked, the device is sterilized by superheated steam and pressurized by sterile air (col. 5 lines 10-14). Also, for claim 23 the air used by Creed in the sterilization process can be a mixture of air and ozone (col. 5 lines 14-15). This solves the problem of sterilizing the culture containers of Hutchins. Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to employ the sterilization apparatus as suggested by Creed within the teachings of Pieler and Hutchins in order to sterilize the trays. The suggestion for doing so at the time would have been in order to sterilize the package-laden trays and cool the trays in a sterile environment (col. 1 lines 4-6).

20. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pieler et al. (WO0 91/01365) in view of Hutchins et al. (US 5,955,373) and in further view of Takagi et al. (JP2001-238663).

21. Hutchings is silent regarding a controller for controlling the pressure within the incubator. Rodgers does imply that the pressure within the incubator is controlled ([0079]; [0083]), but is silent about a specific controller.

22. Takagi teaches a method for culturing cells and tissues that minimizes contamination through a controlled environment. For claim 24, Takagi teaches the pressure within the autoclave at a pressure of 2 atmospheres while sterilizing the culture device (page 2 [0005] lines 4-6 of machine translation). Takagi further demonstrates that a pressure controller for monitoring and adjusting the pressure within a chamber was known at the time of the invention (page 7 [0132] of translation). At the time of the invention, it would have been obvious to one of ordinary skill in the art to employ the pressurized autoclave as suggested by Takagi within the teachings of Pieler and Hutchins in order to have the pressure within the autoclave to be higher than the external pressure. The suggestion for doing so at the time would have been in order to prevent contamination of the culture after disassembling the culture device (page 2 [005] lines 3-4 of machine translation).

23. Claims 29, 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pieler et al. (WO0 91/01365) in view of Hutchins et al. (US 5,955,373) and in further view of Izawa et al. (US 4,556,639).

24. Pieler and Hutchins are silent regarding a pressing unit that applies a magnetic or mechanical force to the culture medium.

25. Izawa discloses a method for removing cells from a culture dish that involves applying a force to the cell culture within the container. For claims 29, 31 and 32, Izawa discloses that a pair of rams (rams 110 & 112) apply a force or pressure to the container and the upward force of the rams is resisted by a buffer member (spring 118) which presses down upon the lid (col. 2 lines 30-32, 34-36). The application of a force to the cell culture, for some types of cells, replicates the force vectors applied to the cells if grown *in vivo*. Therefore, it would have been obvious to one of ordinary skill in the art to employ the pressing means as suggested by Izawa in order to apply a force to the culture chamber of Pieler and Hutchins. The suggestion for doing so at the time would have been in order to peel the culture medium off of the dish (col. 2 lines 44-46) and to replicate *in vivo* conditions for the cells.

26. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rodgers et al. (US 2005/0037485 A1) in view of Hutchins et al. (US 5,955,373) and in further view of Sawamura et al. (U.S. 4,090,921).

27. Hutchins discloses a pipette system for discharging a liquid and Pieler discloses a fluid transfer system. Both references are silent regarding a sterilized tube. Sawamura teaches an automatic cultivating apparatus used for the cultivation of tissues or cells with the ability to maintain a pre-determined atmosphere via atmospheric controls. Furthermore, the tissues or cells are inserted into a plurality of empty

cultivating containers which will be filled with nutrient solution (col. 4 lines 57-59). Also, the nutrient solution is contained within a trough which is connected to a tube which is further connected to a discharge nozzle (col. 4 lines 5-7, Fig. 3 elements 24, 24d & 25). Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to employ the tube and discharge nozzle as suggested by Sawamura within the teachings of Pieler and Hutchins order to dispense a nutrient solution to the culturing vessel. The suggestion for doing so at the time would have been in order to meter the preferred amount of solution to the dish.

28. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rodgers et al. (US 2005/0037485 A1) in view of Hutchins et al. (US 5,955,373) and in further view of Mishima et al. (U.S. 5,182,193).

29. Pieler and Hutchins do not teach the limitation where the measurement device is equipped with electrodes and the culture is placed in between. Mishima teaches a method for measuring biomass within a bioreactor that includes measuring the electrical capacitance across a pair of electrodes attached to the bioreactor. Furthermore, the cells may or may not be immobilized within the bioreactor (Abstract) and the electrical capacitance is measured across the bioreactor (Fig. 1 element 5). Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to employ the electrodes as suggested by Mishima within the teachings of Pieler and Hutchins in order to measure the electrical capacitance across the bioreactor. The suggestion for doing so at the time would have been in order to measure the on-line quantities of micro-organisms without having to take samples from the tank (Abstract).

30. Claims 38 and 39 rejected under 35 U.S.C. 103(a) as being unpatentable over Rodgers et al. (US 2005/0037485 A1) in view of Hutchins et al. (US 5,955,373) and in further view of Bylina et al. (U.S. 5,914,245).
31. Rodgers and Hutchins do not teach the limitations of claims 38 and 39.
32. Bylina teaches a solid phase enzyme kinetics screener in micro-colonies that permits high-throughput screening of enzyme libraries by time course analysis of single-pixels using adsorption, fluorescence or FRET (fluorescence resonance energy transfer) for detecting optically distinct regions composed of micro-colonies of cells. For claim 38, the tester directs monochromatic light from above the target in order to obtain kinetic and spectral data from the micro-colonies (col. 2 lines 32-33 & col. 5 lines 30-32). The tester of Bylina is fully capable of testing the thickness of a cell. Furthermore, for claim 39 the tester of Bylina analyzes the micro-colonies through either fluorescence (**fluorometry**) or FRET (Abstract) based on the emission from either a donor or acceptor moiety (col. 11 lines 15-17). Therefore, it would have been obvious to one of ordinary skill in the art to employ the enzyme kinetic screener of Bylina within the teachings of Pieler and Hutchins in order to test the cell density of the micro-colonies. The suggestion for doing so at the time would have been in order to increase the throughput of testing and decrease the assay volume (col. 2 lines 5-8).

Response to Arguments

33. Applicant's arguments, see page 7 paragraphs 2 and 3, filed 08/18/2008, with respect to the objection of claims 33 and 35 and the specification in paragraphs 1 and 2

of the Office Action mailed on 03/17/2008 have been fully considered and are persuasive. The objection of claims and specification has been withdrawn.

34. Applicant's arguments, see page 7 paragraphs 3 and 4, filed 08/18/2008, with respect to 35 USC 112 second paragraph rejection of claim 21 in paragraph 4 of the Office Action mailed on 03/17/2008 have been fully considered and are persuasive. The rejection of the claim has been withdrawn.

35. Applicant's arguments, see page 8 paragraph 5, filed 08/18/2008, with respect to 25 USC 102(b) rejection in paragraph 8 of the Office Action mailed on 03/17/2008 have been fully considered and are persuasive. The rejection of claim 21 has been withdrawn.

36. Applicant's arguments, see page 8 paragraph 4, filed 08/18/2008, with respect to the rejection(s) of claim(s) 21, 26-29, 33 and 34 under 35 USC 102 (b) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of based upon Hutchins which discloses an automated culture system with a plurality of compartments divided by a wall with an entry door and Rodgers which discloses an automated culture system that includes sensors for monitoring the environmental conditions within each chamber.

Conclusion

37. Claims 21-24, 26-29 and 31-39 are rejected.

38. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Cremonese (US 4,839,292) discloses a cell culture flask that is contained within a plurality of compartments within an incubator and Iwahi et al (JP3-49676) discloses an automatic culturing system that loads and fills Petri dishes at one end of a conveyor and sends the Petri dishes down a conveyor to various processing stations.

39. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL HOBBS whose telephone number is (571)270-3724. The examiner can normally be reached on Monday-Thursday 7:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/William H. Beisner/
Primary Examiner, Art Unit 1797

/M.L.H./